

Official Title: **Compassion Meditation for Cancer Survivor-Caregiver Dyads**

NCT number: **NCT03459781**

Document Date: **February 10, 2022**

**Project Title:** Compassion Meditation for Cancer Survivor Dyads: Feasibility and Preliminary Efficacy of Cognitively-Based Compassion Training® for Solid Tumor Cancer Survivors and Their Informal Caregivers

#### Investigator Information

Principal Investigator Name, Degree(s): Thaddeus Pace, PhD

Affiliation: ☒ UA ☐ B-UMG

Principal Investigator **UA NetID**: twwpace

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Center:

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#### Advisor contact information (Required for all students and residents)

Name, Degree(s), **UA NetID**:

Contact phone:

Official University Email:

#### Alternate/Coordinator or Co-PI contact information

**\*This individual will receive copies of all correspondence on the study**

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## SECTION 1: REQUIRED SIGNATURES

### 1. Principal Investigator

I will

conduct my study according to the University of Arizona HSPP policies and procedures for research with human subjects.



November 20,  
2017

Thaddeus Pace, PhD

Signature

Date

Print Name

### 2. Advisor (for all students and residents acting as the pi)

I will oversee the student researcher according to the University of Arizona HSPP policies and procedures for research with human subjects.

Signature

Date

Print Name

### 3. Scientific/Scholarly Review (See HSPP Guidance on requirements for Scientific/Scholarly Assessment - include documentation for options A and B with submission materials.)

- a. ☐ Nationally based, federal funding organization (NIH, NSF) subject to full peer review
- b. ☐ Nationally based, non-federal funding organization (March of Dimes, Amer Academy of Pediatrics) subject to peer review
- c. ☐ Locally constituted peer review (signature required)

Signature

Date

Print Name

### 4. Department/Center/Section Review

I have reviewed this application and determined that all departmental requirements are met and that the investigator has adequate resources to conduct the Human Research.

Signature

Date

Print Name/Email

### 5. Responsible Physician (projects involving medical procedures which the pi is not authorized to conduct)

I am a physician licensed by the State of Arizona (or US license for the SAVAHCS). I will be responsible for ensuring that all procedures that are part of this project and that require the attendance of a licensed physician will have a suitable physician present during the procedures. If at any time this is not possible, I will inform the IRB before any procedures are conducted.

Signature

Date

Print Name

## SECTION 2: GENERAL INFORMATION

1. How many Human Research studies does the PI have open?

2

2. How many research staff will be involved in the Human Research?

3

3. What is the expected length of this project?

1.5 years

4. Will the University of Arizona be the coordinating center for a multi-site study?

☒ No

☐ Yes- Complete Appendix C- Multi-Site study

5. Retention of study materials before, during, and after completion of the project:

a. Where will original signed consent and PHI Authorization documents be stored (building name and room)? Location: Office of Nursing Research, CON room 410

b. How long will consents be maintained after conclusion of the project?

☒ 6 years (UA standard) ☐ 6 years after child reaches 18 ☐ Other (explain):

6. Is or will the project be funded by an external funding source? ☒ No ☐ Yes- Complete below:

a. Funding PI: Thaddeus Pace, PhD

b. Proposal Title: Wellness interventions and stress-immune mechanisms in cancer survivors and their caregivers

c. Funder Name: Estate of Jack Challem

d. Total funding amount **OR** per subject amount: \$50,000

e. UAccess Account Information Provide one of the following below:

i. Institutional Proposal #:

ii. Award #:

*Submit complete copy, cover-to-cover, of grant or award. If you need help locating any of the UAccess numbers please call Sponsored Projects at 626-6000.*

7. Is the project funded by a **For-profit** industry sponsor? ☒ No ☐ Yes- Complete required below:

a. IRB Payment eDoc #:

*Please review **HSPP Guidance, Fees for Human Research**, for more information.*

8. Conflict of Interest (COI):

The Principal Investigator hereby affirms that ALL individuals who meet the definition of [investigator](#) for this project in the current *Policy on Investigator Conflict of Interest in Research* have completed the mandatory [Conflict of Interest training](#) and [Disclosure of Significant Financial Interests](#).

☒ Yes

☐ No (explain):

## 9. Additional requirements:

Certain types of research require additional regulatory documentation. Please identify which of the following apply to your project. Complete the appropriate Appendix and submit as part of the submission materials.

- ☐ Appendix A – Children (subjects under 18)
- ☐ Appendix B – Drugs/Devices (A clinical investigation of a drug or device)
- ☐ Appendix C – Multi-Site study (The UA IRB will review research activities for an investigator or research staff not affiliated with the UA who is 'engaged in the research' (e.g. consenting, collecting data, or analyzing identifiable information))
- ☐ Appendix D – Pregnant Women/Neonates
- ☐ Appendix E – Prisoners
- ☐ Appendix F – Waivers of consent, waiver of a signature, or waiver or alteration of PHI
- ☐ Appendix G – Exception From Informed Consent (EFIC)
- ☐ Appendix H – Native American or International Indigenous populations
- ☒ None apply to the proposed study

## 10. Research Site:

Location (Explain):

All procedures for the proposed research will take place at the College of Nursing at the University of Arizona. No UACC resources will be used, including access to the electronic medical record. Participants for this study will be recruited from across Tucson and will either be individuals who have completed their cancer treatments a minimum of 3 months before enrollment in the study, or their informal caregivers (i.e. wives, husbands, adult children, and close friends). We will not recruit participants who are current patients at Banner UMC or the UACC for their cancer treatments.

If research is taking place at B-UMG or AZCC please check the appropriate boxes below:

### Banner – University Medicine Group:

- |   |   |  |
|---|---|--|
| <input type="checkbox"/> Phoenix Campus | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |
| <input type="checkbox"/> Tucson Campus  | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |
| <input type="checkbox"/> South Campus   | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |

*\*Submit a copy of the UAHS Research feasibility review approval*

### University of Arizona Cancer Center:

- |   |   |  |
|---|---|--|
| <input type="checkbox"/> North Campus         | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |
| <input type="checkbox"/> Orange Grove Clinics | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |
| <input type="checkbox"/> Phoenix              | <input type="checkbox"/> Biological specimens | <input type="checkbox"/> Clinical Data |

*\*Submit a copy of the Scientific Review Committee letter*

## SECTION 3. PROJECT NARRATIVE

## 1) Background

Advancements in early detection and treatments have dramatically improved the prognosis for the majority of patients diagnosed with solid tumor cancers. Indeed, recent trend data show that 5-year survival rates are improving for those diagnosed with and treated for colorectal (66%), lung (18.7%), prostate (99%), and breast cancer (women, 90%).<sup>1</sup> Despite these gains, health-related quality of life (HRQOL) impairments remain a significant concern for cancer patients during and after treatment. For example, survivors of different cancers are likely to experience increased depressive symptoms (e.g. colorectal: 28%,<sup>2</sup> lung: 8-31%, ADDIN EN.CITE <sup>3,4</sup> prostate: 18%,<sup>5</sup> and breast: 10-25%, ADDIN EN.CITE <sup>6,7</sup>), fatigue (23-73%, ADDIN EN.CITE <sup>2,8</sup> 98%,<sup>9</sup> 12-21%,<sup>10</sup> and 30-80%, ADDIN EN.CITE <sup>11-13</sup> respectively) as well as anxiety. ADDIN EN.CITE <sup>3,14-18</sup>

Although the focus of interventions to improve HRQOL is usually on the experiences of cancer survivors, close family members and friends who provide supportive care (i.e. informal caregivers) also experience significant HRQOL impairments during and after the time when their loved ones undergo cancer treatment. ADDIN EN.CITE <sup>19,20</sup> Informal caregivers are not just passive bystanders, but instead provide significant supportive care (as much as 60%) to their loved one. ADDIN EN.CITE <sup>21-23</sup> A nascent literature (including work by us) suggests that impairments in caregivers' HRQOL, in addition to directly affecting perceptions of quality of care,<sup>23</sup> are strongly interdependent with and possibly causally linked with the HRQOL impairments experienced by their loved ones who are cancer survivors. For example, work by our group has shown that increased depressive symptoms, anxiety, symptom distress (including fatigue), and negative affect that breast cancer survivors experience are interdependent with the same impairments that their informal caregivers experience.<sup>24</sup> We have found the same interdependence/ causal linkage of HRQOL impairments in prostate cancer survivors and their informal caregivers.<sup>25</sup> Together these findings suggest that informal caregivers are much more than a "social backdrop" to cancer and its treatment.<sup>24</sup> Instead, HRQOL is shared by both members of a cancer survivor dyad by way of "emotional contagion," or the multilevel phenomenon whereby stimuli from one individual results in a complimentary emotional or behavioral state in another individual.<sup>26</sup> The scientific premise of the interdependence between a survivor's and caregiver's HRQOL demands that interventions be developed and tested that are directed at both members of the dyad. One such intervention, CBCT® (Cognitively-Based Compassion Training) has been tested by us in cancer survivors (see justification and feasibility) and will now be extended to informal caregivers.

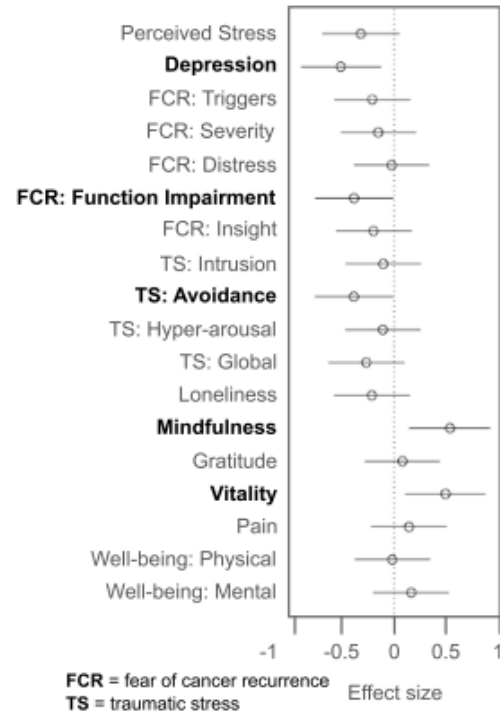
CBCT® is an established 8-week meditation-based program developed by Lobsang Tenzin Negi, PhD at Emory University that has already been shown by us to have HRQOL benefits for breast cancer survivors.<sup>27</sup> CBCT® cultivates empathy and prosocial capacity and enhances perceptions of social connection and positive emotions for others. CBCT® is an iterative program, in that skills learned each week build upon each other. The program begins by teaching mindfulness practices for mental stability and non-reactive awareness, but then goes on to facilitate self-compassion, positive emotions, and feelings of social connectivity through compassion-based techniques of actual or imagined experiences of desired emotional states. Effectiveness of CBCT® was found in several different populations, with multiple health-related outcomes. ADDIN EN.CITE <sup>27-33</sup> We have already shown in a published pilot study that CBCT® had beneficial effects on dimensions of HRQOL in breast cancer survivors including symptoms of depression, fear or cancer recurrence, and vitality (related to the inverse of fatigue).<sup>27</sup> Pilot data with CBCT® in breast cancer survivors were obtained from a 2-arm trial conducted by our group (Dodds and Pace).<sup>27</sup> Breast cancer survivors who completed cancer treatments except for aromatase inhibitors or tamoxifen were randomized to CBCT® (n=16) or a wait list control (n=17). In favor of acceptability and feasibility of CBCT® for cancer

survivors, retention in CBCT® over 8 weeks was 75%, and 100% of those who attended CBCT® completed the post-intervention assessments.<sup>27</sup> Compared to controls at post-intervention, the CBCT® group showed significant improvements in depressive symptoms (CES-D-10), functional impairment associated with fear of cancer recurrence, and vitality as well as avoidance of intrusive thoughts and mindfulness (**Figure 1**). These preliminary findings suggest that CBCT® is feasible and may promote positive change with respect to key aspects of HRQOL in cancer survivors. **We are now** proposing to extend these findings to survivors of others cancers, and **to pilot the program in a form where cancer survivors will take part in the CBCT® program in training sessions along with their informal caregivers**. We plan to determine the acceptability and feasibility of CBCT® for cancer survivor-caregiver dyads, assess changes in HRQOL (as we did in our study with only survivors) in both survivors and caregivers, and also assess in a preliminary manner how CBCT® for survivor-caregiver dyads may have a beneficial effect on stress-related biomarkers of inflammation and cortisol, and healthcare adherence.

There is good justification for examining stress-related physiological function by way of stress biomarkers in cancer survivor-informal caregiver dyads who are participating in a contemplative or behavior interventional study. Considerable evidence from research over the last two decades has linked HRQOL impairments in cancer survivors to changes in stress-related physiological function, including diurnal cortisol production as well as inflammation. Inflammation is measurable at multiple levels including circulating (i.e. blood concentrations) of inflammatory mediators such as cytokines (interleukin [IL]-1beta, IL-6 and tumor necrosis factor).<sup>34</sup> Breast cancer survivors have been found to have increased circulating concentrations of key inflammatory biomarkers that positively correlated with fatigue. ADDIN EN.CITE<sup>35-41</sup> Severity of major depression features have also been associated with inflammatory biomarkers, including IL-6, in cancer survivors.<sup>42</sup> With further regard to the ways that inflammation may drive the symptoms experienced by cancer survivors, a rich literature suggests that inflammatory cytokines undercut neurotransmitter metabolism and function in key brain regions, resulting in depression and fatigue. ADDIN EN.CITE<sup>50,51</sup> Taken together, these findings strongly suggest that inflammation plays an important role in the pathophysiological mechanisms of impairments in many dimensions of HRQOL experienced by cancer survivors. With respect to HRQOL impairments experienced by informal caregivers, there is also a rich science on how inflammation is causally linked with quality of life impairments experienced by non-survivors as well. Also part of the rationale for examining inflammation in informal caregivers undergoing wellness interventions is that HRQOL impairments have been found to be linked between cancer survivors and informal caregivers.<sup>24</sup> The same HRQOL impairments have been associated with inflammation.

Multiple studies suggest that increased inflammation may interact with abnormal cortisol activity in the context of HRQOL impairments experienced by cancer survivors.<sup>52</sup> Significant distress in breast cancer survivors has been associated with dysregulation of the hypothalamic-pituitary adrenal (HPA) axis, most frequently manifested as reduced variation in cortisol from morning (when cortisol is

**Figure 1.** Standardized effect sizes of differences between CBCT® and control for post-intervention outcomes in breast cancer survivors.<sup>1</sup>



normally high) to evening (when cortisol is normally low).<sup>53</sup> Psychological distress has been found to be associated with flattening of the diurnal cortisol slope in numerous patient populations, including those with cancer. ADDIN EN.CITE <sup>54-57</sup> Previous research has documented that flatter cortisol slope, or abnormal diurnal cortisol rhythm (DCR), has been associated with fatigue<sup>58</sup>, tumor progression, reduced survival ADDIN EN.CITE <sup>59,60</sup>, and depression, ADDIN EN.CITE <sup>56,61</sup> and in breast cancer, with negative psychosocial and disease outcomes. ADDIN EN.CITE <sup>62-65</sup> We have recently observed that a flatter cortisol rhythm across the day (lower cortisol in the morning and higher cortisol at night) is associated with greater fatigue in breast cancer survivors (Figure 2). Following psychosocial intervention, Giese-Davis and colleagues found that emotional expression within breast cancer therapy was associated with less aberrant cortisol slopes.<sup>55</sup> Thus, treatments targeting psychological distress may result in a DCR comparable to that of individuals without cancer. ADDIN EN.CITE <sup>53,56</sup> Regarding the role that cortisol system activity may play in HRQOL impairments experienced by cancer survivors, Thornton and colleagues found that stress-related neuroendocrine hormones including cortisol predicted pain, depression, and fatigue.<sup>66</sup> Together these findings provide a strong rationale for choosing DCR as a marker of disease-relevant cortisol activity in the context of HRQOL impairments experienced by cancer survivors. Available evidence also suggests that DCR alterations (i.e. flattening of the cortisol slope) also associate with depression, distress, and fatigue in non-survivors. In the current investigational study we will therefore investigate biomarkers of inflammation and DCR in both cancer survivors and informal caregivers undergoing CHE or CBCT®.

In addition to dimensions of HRQOL and stress-related physiological function, another concern about the well being of solid tumor cancer survivors is the degree to which cancer survivors adhere to healthcare recommendations (including following cancer survivorship plans). In a chronic illness model, cancer survivorship requires lifelong adherence to survivorship care, and adherence may consist of several dimensions including *appropriate use of health services*. In turn, health services utilization requires having *access to available health care resources*, but are further mediated by physical, psychological, psychosocial, and economic factors in the patient. For example, adherence may be challenged when other chronic, *co-morbid conditions* are present, when patients experience *depression or anxiety*, or when social support is limited. In addition, cancer survivors report that adequate *health insurance coverage*, a major barrier to service access and utilization, is one of their most important health care needs.

Factors within the health care system may also affect adherence. For example, among cancer patients, *receiving treatment summaries and survivorship care plans* supports self-management while also providing information to primary care physicians involved in follow-up care. Studies show that receiving a verbal explanation of follow-up instructions is significantly associated with higher self-efficacy scores, and these in turn are significantly associated with lower emergency room visits and hospitalizations. This also holds true for other chronic diseases, such as diabetes or arthritis.

One psychological factor in adherence is a degree of patient motivation and activation. The importance of the patient as an active, engaged participant in their own cancer survivorship and chronic disease management has received growing attention in the past decade, so much that the US Centers for Medicare and Medicaid Services assessed patient activation and engagement in its recent evaluation of innovative Pioneer Accountable Care Organizations (ACOs).

*Activated patients* are those with the motivation, knowledge, skills, and confidence to make effective decisions in managing their health. Those with low activation are typically passive recipients of care and do not believe in the need for an active patient role. Those who are highly activated are proactive about their health and engage in many recommended health behaviors. Activation,



however, is not either/or. A widely used developmental model of activation involves four stages: (1) believing the patient role is important, (2) having the confidence and knowledge necessary to take action, (3) actually taking action to maintain and improve one's health, and (4) staying the course even under stress (Hibbard et al. 2004; Hibbard et al., 2005). See **Figure 3**.

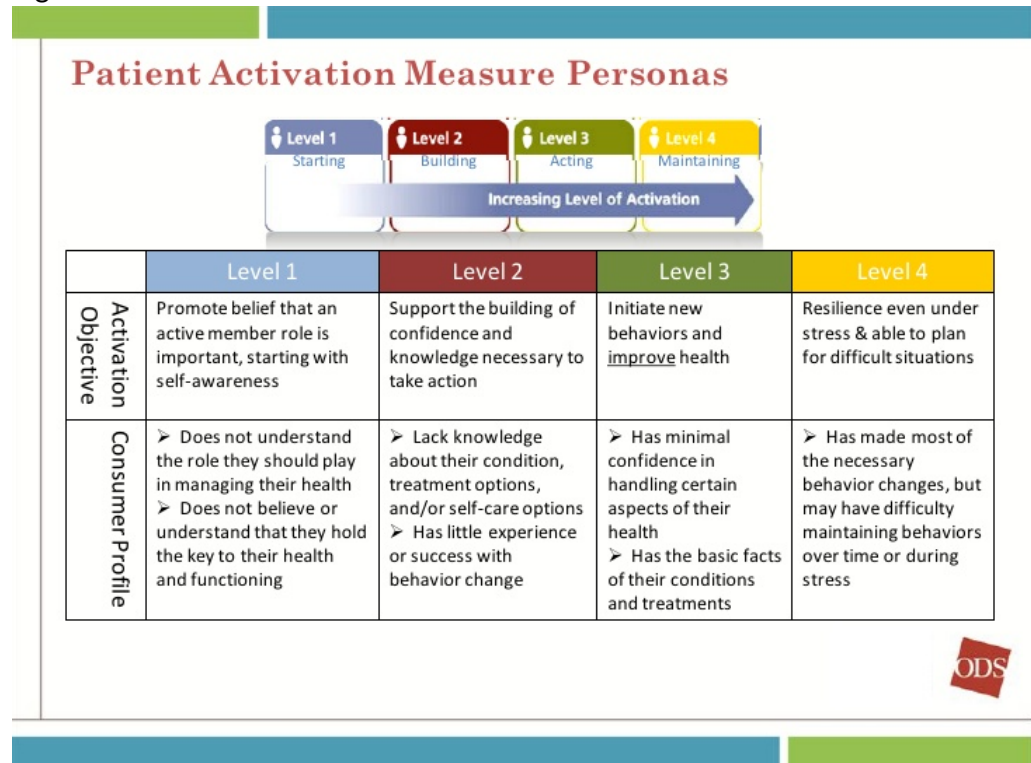
Correlational studies have found patient activation to be related to healthy lifestyle behaviors (e.g. physical activity, eating fruits and vegetables), appropriate use of health care services (e.g. having fewer hospitalizations), and self-management of chronic conditions (e.g. diabetic eye examinations, recording blood pressure readings, HbA1c control).

Other studies show patient activation to be a modifiable characteristic, and that interventions can increase self-management capacities and health services use. For example, among patients in a community health center, a brief activation intervention helped patients have more

effective encounters with physicians. Among community mental health clinic patients, a 3-session activation intervention improved health-related decision-making. Further, patients showed improvements in activation even when an intervention was delivered online.

In addition to HRQOL outcomes, in the current pilot study we will also explore patterns of and barriers to health care adherence in solid tumor cancer survivors and their informal caregivers. Exploration of this dimension is limited only because of the short time frame of the study and the high likelihood that participants will have too few scheduled appointments in that period with which to adequately assess health behavior change. Further, along with changes in dimensions of health-related quality of life and on biomarkers of inflammation and diurnal cortisol rhythm, we AIM to determine the efficacy of CBCT® on improved patient activation, an important ingredient in chronic care management. This information will not only help us determine the efficacy of CBCT® on patient activation, but also the role of activation on health care adherence in a full-scale study with less restrictive time constraints in the future.

Figure 3.



## 2) Purpose

The overarching purpose of the proposed research is to determine the feasibility, acceptability, and preliminary efficacy of Cognitively-Based Compassion Training (CBCT®) compared to a cancer health education (CHE) attention control on dimensions of health-related quality of life (HRQOL), biomarkers of inflammation and diurnal cortisol rhythm, and healthcare utilization-related endpoints including healthcare-related patient activation. To address this goal, we present the following aims:

**Aim 1: To determine the feasibility, acceptability, and obtain preliminary evidence of efficacy (as reflected by the effect sizes) of an 8-week CBCT® (Cognitively-Based Compassion Training) program for survivors of solid tumor cancer and their informal caregivers to impact health-related quality of life outcomes.** The objective of this aim is to determine feasibility and acceptability of CBCT® for cancer survivor-caregiver dyads compared to CHE, and to also obtain preliminary measures of pre to post intervention change on HRQOL including psychological (depression features\*, anxiety features, negative affect), physical (fatigue), social (empathy, feelings of social isolation, dyadic function), and spiritual (self-compassion) domain as well as global well-being. The endpoint noted above (\*) is primary, all others are secondary.

**Hypothesis 1:** Randomization to CBCT® will result in greater changes/ improvement in domains of HRQOL from before to after the intervention programs than randomization to CHE.

**Aim 2: To obtain preliminary evidence of efficacy (as reflected by the effect sizes) of an 8-week CBCT® program for survivors of solid tumor cancer and their informal caregivers on stress-related biomarkers of inflammation and diurnal cortisol rhythm.** The objective of this aim is to obtain preliminary measures of pre to post intervention change on stress-related biomarkers of inflammation (plasma interleukin [IL]-6, IL-1 beta, tumor necrosis factor (TNF)- alpha, as well as diurnal saliva cortisol change in survivor-caregiver dyads randomized to CBCT® compared to survivor-caregiver dyads randomized to CHE.

**Hypothesis 2:** Randomization to CBCT® will result in greater change in inflammatory cytokines (decreased IL-6, IL-1beta, TNF-alpha) from before to after the intervention program than randomization to CHE.

**Hypothesis 3:** Randomization to CBCT® will result in a greater dynamic change in saliva concentrations of cortisol from morning to evening (i.e. diurnal cortisol rhythm) from before to after the intervention programs than randomization to CHE.

**Aim 3: To explore health care adherence in both survivors of solid tumor cancer and their informal caregivers, and obtain preliminary evidence of efficacy of the 8-week CBCT® program (as reflected by the effect sizes) on patient healthcare-related activation.** The objective of this aim is to obtain preliminary measures of pre to post intervention change in healthcare activation (i.e. intent to use cancer-related survivorship plans [survivor] and management plans of other chronic conditions [survivor and caregiver) in survivor-caregiver dyads randomized to CBCT® compared to survivor-caregiver dyads randomized to CHE.

**Hypothesis 4:** Randomization to CBCT® will result in greater patient activation than CHE from before to after the intervention programs.

**Aim 4: To explore the interdependence of solid tumor cancer survivor and informal caregiver health-related quality of life from before to after CBCT® (Cognitively-Based Compassion Training).**

The objective of this aim is to statistically determine the degree to which changes of HRQOL measures, biomarkers of inflammation, or diurnal cortisol rhythm in survivors predicts changes in caregivers (or vice-versa).

**Hypothesis 5:** Randomization to CBCT® will result in greater interdependence on study outcomes between survivors and caregivers than randomization to CHE.

### 3) Lay Summary (approximately 400 words)

Survivors of solid tumor cancers and their informal caregivers (family members or friends) experience significant impairments in health-related quality of life (HRQOL) including disruptions in psychological, physical, social, and spiritual well-being. Our prior work demonstrates that impairments in depression, anxiety, fatigue, and negative affect experienced by cancer survivors across time are strongly related to, or interdependent with, those experienced by their informal caregivers. These findings suggest that interventions directed simultaneously toward both members of the cancer survivor-caregiver dyad may be especially impactful in improving HRQOL in cancer survivors and informal caregivers. Although a number of interventions have been developed and tested to support the survivor or the caregiver, few have attempted to simultaneously intervene with both to improve HRQOL within the collective survivor-caregiver dyad. CBCT®, Cognitively-Based Compassion Training (already piloted by members of this team with breast cancer survivors, is an 8-week manualized meditation-based program that starts with attention and mindfulness training and builds to contemplation about compassion for the self and others. It differs from other meditation interventions in that it directly enhances self-compassion, feelings of social connection, empathy for others, and equanimity and by doing so lessens emotional suffering. Our recent findings suggest that CBCT® may reduce depressive symptoms, fear of cancer recurrence, and improve vitality in breast cancer survivors. The proposed pilot feasibility study builds upon this work to intervene with caregivers in addition to survivors of solid tumor cancers. The major aim of the proposed project is to test the feasibility and acceptability of CBCT® for survivors of solid tumor cancer and their informal caregivers after the end of cancer treatment. The project will also determine in a preliminary manner whether or not CBCT® has a positive impact on different measures of HRQOL (e.g. features of depression and anxiety, fatigue, social isolation), stress-related biomarkers of inflammation and cortisol, and assessments related to healthcare utilization (patient healthcare-related activation). Using the actor-partner interdependence model, the project will also explore the interdependence of the solid tumor cancer survivor and informal caregiver HRQOL outcomes from before to after CBCT®. If feasibility and acceptability are established in this research, a future larger trial will be warranted and appropriately powered to formally test the efficacy of this dyadic CBCT® intervention. Evidence-based programs such as CBCT® may fill the gap in supportive psychosocial oncology care directed toward both members of the survivor-caregiver dyad, as opposed to programs directed at the either alone. We believe that CBCT® is a particularly promising program because it may be effective at enhancing both the individual and the collective empathy shared by a cancer survivor and his or her informal caregiver.

### 4) Setting of the Human Research

All procedures for the proposed research (except saliva collection) will be completed at the University of Arizona College of Nursing: including blood draws, self-report assessments, and the 8-week intervention classes (CBCT® and CHE). There will be three assessment time points: before the 8-

week interventions (T1), immediately after the 8-week intervention classes (T2), and then again 3 months later (T3). Blood samples will be drawn in the Research Suite phlebotomy room (CON 418C), and paper Scantron questionnaires will be completed in the Research Suite conference room (CON 418A). The weekly CBCT® sessions will take place in CON 349, and the weekly CHE sessions in CON 416.

Saliva collection will take place in participants' homes per the Saliva Instructions form (attached).

## 5) Resources available to conduct the Human Research

- **Facilities**

All study procedures (assessments and interventions) will be completed at the University of Arizona College of Nursing where Dr. Pace (PI) is member of the faculty. Processing and analyses of all biological samples will take place in the Biological Core Laboratory at the College of Nursing, where Dr. Pace already conducts work for other projects according to biosafety and chemical safety protocol plans already approved at the University of Arizona.

- **Research Personnel Training Plan**

All study personnel have already undergone human subjects research training via the CITI Program. Dr. Dodds has received training from the CBCT® Teacher Certification Program at Emory and takes part in periodic refresher seminars. She also periodically consults with CBCT® program faculty and staff including Dr. Negi, the creator of CBCT®, as well as Tim Harrison, Director of the CBCT® Training Program.

## 6) Study Population

This study will enroll survivors of solid tumor cancers who have completed cancer treatment (except for hormonal therapies) and their informal caregivers. Participants of both genders and all racial/ ethnic backgrounds will be included.

**Cancer survivor inclusion criteria:** **1)** age 21 or older, **2)** have a solid tumor cancer diagnosis, **3)** have completed treatments (surgery, radiation, chemotherapy) except for hormonal therapies (e.g. aromatase inhibitors, androgen suppression therapy) a minimum of 3 months and a maximum of 10 years before starting CBCT® or CHE, **4)** able to speak and understand English, and **5)** able to travel to a centralized location to attend CBCT® or attention control classes.

**Cancer survivor exclusionary factors:** **1)** diagnosis of major mental illness, **2)** nursing home resident, and **3)** ongoing compassion meditation practice (as determined by the Principle Investigator).

**Informal caregiver inclusion criteria** will be: **1)** named by the cancer survivor, **2)** age 21 or older, **3)** able to speak and understand English, **4)** cognitively oriented in time, place, and person, and **5)** able to travel to a centralized location to attend intervention classes with their solid tumor cancer survivor. Informal caregivers will be excluded if they have ongoing compassion meditation practice (as determined by the Principle Investigator).

In addition to these criteria, either the cancer survivor or the informal caregiver must report at least **mild anxiety** (PROMIS anxiety 4-item raw score > 6) and/ or **mild depressive symptoms** (PROMIS anxiety 4-item raw score > 6) to be randomized to either intervention arm.

The sample size for this feasibility study (N=48 dyads [96 participants total]; CBCT® about n=24, CHE attention control about n=24) is based on the number of cancer survivor-caregiver dyads that are projected to meet inclusion criteria for depressive and/or anxiety symptoms who will complete the entire study protocol. This feasibility study will not formally test hypotheses but will determine estimates of the effects sizes for future work, thus formal hypothesis-based sample size determination is not applicable. The proposed sample size will yield estimates of and the confidence intervals for the effect sizes for the improvements in primary outcomes in physical, psychological, and social HRQOL (depressive symptoms, anxiety, fatigue, negative affect, empathy, and dyadic function) for those randomized to CBCT® versus the CHE attention control. We will also estimate effect sizes for stress-related biomarker outcomes. The rigor of the proposed pilot RCT design (i.e. having the CHE attention control) will secure the attribution of the effects to the intervention.

## 7) Recruitment Methods and Consenting Process

### a. Recruitment Process:

Participants for the study will be recruited by the PI (Pace) and the study coordinators (Hadeed/ Figueroa/ Hofacre) from cancer advocacy organizations in metropolitan Tucson. The PI, study coordinators, and others on the research team already have strong collaborative relationships with these advocacy organizations (see letters of support).

We may use additional recruitment materials in the future, including a recruitment flyer (see Appendix). This flyer will be distributed to partnering cancer advocacy organizations (see letters of support) as well as at the University of Arizona Cancer Center.

A recruitment script (version already approved) will be read to prospective participants before they are presented with a consent form.

### b. Informed Consent:

Participants will be consented in person and with a printed consent form (see attached) by the study coordinators or the PI, either in the community or at the College of Nursing. If consented in the community, a public place such as a coffee shop, restaurant, or community center may be used. If at the College of Nursing, a private conference will be used. During the consenting process participants will be made aware that the study involves an 8-week intervention and several self-report assessments, and blood sampling by venipuncture.

## 8) Research procedures involved in the Human Research

Over the course of the study we will randomize about 24 survivor-caregiver dyads to CBCT®, and about 24 dyads to the CHE attention control. We will conduct the study in 3-4 cohorts, with about equal number of dyads randomized to CBCT® and CHE in each cohort. Randomized dyads will include cancer survivors and informal caregivers with at least mild depressive or anxiety symptoms (see **Study Population**, above). The research procedures are elaborated below in chronological order of when they will occur for each study cohort. The study will consist of four major phases after recruitment/ screening/ consent:

1. Baseline (pre-intervention) assessments
2. Intervention phase
3. 8-week (post-intervention) assessments
4. 3-month (post intervention) assessments

- **Assessments - Baseline (pre-intervention)**

After successful recruitment, screening, and consent we will invite solid tumor cancer survivor-informal caregiver dyads to the College of Nursing for the baseline assessment. Shortly after arrival blood will be collected from participants before starting self-report questionnaires. Blood will be drawn in order to obtain plasma and peripheral blood mononuclear cells (PBMCs). Blood (2 X 7 milliliters) will be collected by venipuncture into EDTA-coated vacutainer tubes by the (TBA) study phlebotomist, and then immediately processed to obtain plasma (centrifugation at 1,030 rcf at 4 °C for 10 minutes before freezing at -80 °C), or PBMCs (blood will be dilute 1:1 with sterile saline, loaded onto a ficol-hypque gradient before centrifugation at 1,500 rcf for 10 minutes at room temperature, followed by isolation of leukocytes (PBMCs), then washing of cells with 1 X PBS before storage in freezing serum [fetal bovine serum + 10% DMSO] at -80 °C).

After completion of baseline self-report questionnaires (including demographics questionnaire with height and weight) and before departing the College of Nursing we will distribute to all survivor-caregiver dyads home saliva collection kits in order to assess cortisol diurnal rhythm. The saliva collection kits (see Appendix for kit Saliva Instructions form) will instruct survivors and caregivers to collect saliva in the home setting on two consecutive days in the morning at waking, and again in the evening after dinner and about 2 hours before bedtime. These samples will be returned to the lab at the College of Nursing, and will be batch analyzed for concentrations of cortisol to assess diurnal cortisol rhythm (see **Laboratory Procedures** below for assay details).

After providing the saliva collection kit, we will next ask survivor-caregiver dyads to complete self-report assessments. Self-report instruments to be completed will assess different dimensions of **health-related quality of life** (HRQOL)(those marked by a \* are primary). Please see the Appendix for the complete self-report packet. Each of the questionnaires are described immediately below:

### **Health-Related Quality of Life** self-report instruments

⇒**Depressive\* and anxiety symptoms (psychological HRQOL):** PROMIS-short forms 8-items: depression and anxiety. These short forms are already in use by members of the study team (Pace) and like other PROMIS forms have evidence for reliability and validity. PROMIS measures were developed with various techniques including Item Response Theory (IRT). ADDIN EN.CITE <sup>67-70</sup>

These forms will minimize participant burden relative to more traditional scales (e.g. CES-D).

⇒**Negative affect (psychological HRQOL):** 10-item Positive and Negative Affect Schedule (PANAS). The PANAS contains positive and negative affect subscales. Reliability is good (0.86-0.90 for positive scale, 0.84-0.87 for the negative scale).<sup>71</sup>

⇒**Fatigue (physical HRQOL):** PROMIS: fatigue will be used to capture physical and emotional components of fatigue. The BFI is a self-report instrument containing 9 items designed for the rapid assessment of fatigue in cancer patient and takes <5 minutes to complete.<sup>72</sup>

⇒**Empathy (social HRQOL):** Interpersonal Reactivity Index (IRI). The IRI was designed to assess empathy, defined as the reactions of one individual to the observed experiences of another. The IRI comprises four sub-scales that measure a component of empathy: perspective-taking, empathic concern, personal distress, and fantasy. The IRI has demonstrated good validity and reliability and has been used widely since its creation.<sup>73-75</sup>

⇒**Social connection (social HRQOL):** Social Connectedness Scale, Revised (SCS-R). The SCS-R is based on the original Social Connectedness Scale that was developed to measure perceived social connectedness.<sup>76</sup> The revised scale, SCS-R, addresses psychometric limitations in the original and consists of 20 items.<sup>77</sup>

⇒**Dyadic function (social HRQOL):** Relationship Assessment Scale (RAS). Quality of relationship will be measured using the RAS, a 7-item scale designed to measure general relationship satisfaction. Respondents answer each item using a 5-point scale ranging from 1 (low satisfaction) to 5 (high satisfaction).<sup>78</sup>

⇒**Self-compassion (spiritual HRQOL):** Neff Self-Compassion Scale (NSCS). The NSCS measures the construct of self-compassion, defined as being kind to oneself instead of harshly critical in situations of pain or failure; perceiving experiences as part of the larger human condition; and being aware of painful thoughts and feelings without over-identifying with them.<sup>79</sup> This 26-item scale has good test-retest reliability (0.93).<sup>80</sup>

⇒**Global HRQOL:** Defined as subjective well-being related to life happiness/ satisfaction, global HRQOL will be measured using the Quality of Life Index (QLI) developed by Ferrans and Powers and is suitable for cancer and non-cancer populations. Generic version will be used for caregivers, and cancer version will be used for survivors.<sup>81</sup> The QLI reflects both satisfaction and importance of various aspects of life, using 30 items for each. Importance ratings are used to weight satisfaction responses, so scores reflect satisfaction with aspects of life that are valued by the individual. Total score summarizes multiple HRQOL domains.

### Healthcare adherence self-report instruments

⇒**Health services utilization:** We operationalize health services utilization as appointment-keeping for oncologic, primary care, and non-cancer specialty care (if needed). Dimensions assessed on the Healthcare Utilization Self-Report Questionnaire, developed by us, follow approaches used in previous studies of cancer survivors (Kirchhoff et al., 2012) and of chronic care patients (Lorig et al., 2001) and include:

**o Access to care:**

- Having adequate health insurance coverage and the ability to meet out of pocket (OOP) health expenses;
- Having designated, identifiable providers for cancer care, primary care, and other non-cancer specialty care; and,
- Having received a cancer survivorship care plan (for the survivor).

**o Health service appointment-keeping:**

- Appointments made and kept in the prior 2 months with 3 types of health providers, cancer care providers, primary care providers, and other non-cancer medical specialists. If unable to keep an appointment(s), respondents select from a list of common reasons.

**o Receipt of routine preventive services:**

- In the past year, receipt of an annual physical exam; screenings for hypertension, osteoporosis (women), mammogram (women), Papanicolaou/PAP test (women), prostate cancer (men); flu shot; and, dental check-up or dental care

**o Urgent Care, Emergency Room, and Hospital Services**

- Receipt of services in the past 2 months at an urgent care center, a hospital emergency room (ER), or inpatient admission to a hospital for at least one night.

**Biological Core Laboratory Procedures.**

Plasma and PBMCs will be batch analyzed later (i.e. after collection of all samples from a given cohort / across all time points [baseline, 8-week, and 3-month; see below]). Concentrations of interleukin (IL)-6, IL-1beta, and TNF-alpha in plasma will be determined using a high-sensitivity magnetic bead multiplex from R&D Systems. The PI's laboratory at the College of Nursing has experience with multiplex assays for cytokines and has found good agreement between cytokines concentrations determined using multiplex assays and high-sensitivity ELISA. There is no genetic analyses part of this study. This study will not involve genetic tests of any kind, including gene expression of gene polymorphisms analyses.

Saliva concentrations for cortisol will be determined using ELISA kits from Salimetrics (State College, PA) according to manufacturer instructions.

● **Interventions**

Within 2 weeks of the baseline assessment study participants will begin either 8 weeks of CBCT® or 8 weeks of CHE, depending on randomization. Study group will be revealed to study participants and study staff after the completion of the baseline assessment. Sealed envelopes will be used in order to obtain dyad group assignment immediately at the conclusion of the baseline assessments.

Upon randomization to either the CBCT® or CHE groups participants will be given a booklet, "Survivorship and Surveillance Guidelines", and another booklet, "Healthy Behaviors for a Healthier Life." Although these booklets will not be referred to directly throughout CBCT® or CHE, participants will be encouraged review them and ask questions about the content of these booklets throughout the study. These booklets are being included because they may have an indirect effect on measures



of health care adherence/ utilization in both the CBCT® and CHE groups.

### **CBCT® (Cognitively-Based Compassion Training)**

CBCT® was designed at Emory University by Lobsang Tenzin Negi, PhD. CBCT® is a secular adaptation of techniques derived from traditional Tibetan Buddhist methods for cultivating compassion known as *lo-jong*.<sup>82</sup> Translated as “thought transformation”, *lo-jong* is considered to be an analytical meditation, one that actively incorporates intellectual analysis into meditation practice with a goal of complete reorientation away from egoistic self-centeredness (i.e., “self-cherishing”) toward altruism or “other-cherishing”.<sup>83</sup> From the *lo-jong* perspective, self-centered thought and behavior cause suffering for oneself and others, while other-centered, altruistic thoughts, emotions, and actions benefit oneself and others. Over the course of **8 weeks** there will be a total of **8 CBCT® sessions, one session per week**, led by the CBCT® instructor (Dodds). Participating dyads will attend the weekly CBCT® classes together, which we believe will be critical to make concepts and empathy salient for survivor and informal caregiver in each dyad. Each weekly session will last for 120 minutes and will begin with brief meditation to focus attention. This will be followed by a didactic phase in which the instructor will articulate content and goals of the current week, after which a group discussion led by the instructor will take place. A session will end with a 20-30 minute meditation guided by the instructor. Of note, the instructor (Dodds) has worked with cancer survivors previously,<sup>27</sup> and is a cancer survivor herself. In between weekly meetings, dyads will be encouraged to practice a minimum of 10 minutes per day at home, and together as a dyad if possible. Our previous work suggests that participants who practice an average of 3.1 sessions per week (10 minutes minimum per session) tend to exhibit meaningful changes in various outcomes including depressive symptoms, self-compassion, and inflammatory markers. ADDIN EN.CITE <sup>27-33</sup> Home practice will be encouraged by providing dyads with printed narrative summaries of weekly lessons, as well as guided meditation audio recordings created by the Emory CBCT® program. Participants will be asked to complete a CBCT practice log (see attached CBCT Practice Log form) in order to encourage practice, and to gather information on their engagement with CBCT. Below is a summary of topics/work (by week) of the CBCT® protocol. This program has been studied previously with other populations, including breast cancer survivors: ADDIN EN.CITE <sup>27-33</sup>

The course is divided into six modules, taught across 8 sessions that meet for 120 minutes, plus time for personal practice between sessions. All sessions combine lecture, discussion, experiential exercises, and reflective practice.

#### → Class Meeting 1 – Introduction and Foundational Practice

In the first session, the instructor presents an introduction and overview, which informs the participants about the following:

- Develop a working definition of compassion (as distinct from empathy) and how it can be cultivated systematically with a skill-building approach.
- Explain researched-based and theoretical benefits of compassion, including improved empathic accuracy, increased happiness and activation of the brain’s pleasure circuitry, a multitude of health benefits, and increased patient outcomes and satisfaction.
- Delineate the core concepts of the Emory University protocol CBCT® (Cognitively-Based Compassion Training), including sustained attention, self-compassion, equanimity, impartiality, interdependence, and gratitude.

- What “cognitively-based” means and how the program may differ from other types of meditation/cognitive retraining participants may have engaged in.
- Foundational Practice: Resting in a Moment of Nurturance

→ Class Meeting 2 – Module I: Attentional Stability and Clarity

This class presents Module I: Developing Attentional Stability and Clarity. The initial practice trains attentional stability in order to improve mental stability and clarity; typically, this is done by placing and retaining focus on the unfolding sensations of the breath and by learning to relate to distractions with greater equanimity.

→ Class Meeting 3 - Module II: Cultivating Insight into the Nature of Mental Experience

Still rooted in the present moment, the focus shifts to how mental experience unfolds from moment to moment. The goal is to pay attention without pushing away this mental activity or becoming overly involved in it. This practice develops a flexible responsiveness to inner experience, insight into habitual mental patterns, and increased calmness of mind.

→ Class Meetings 4 and 5 -- Module III: Self-compassion

Using insights from Module II, this practice looks closely at how mental patterns and inner perspectives contribute to a sense of well-being. Lasting relief from difficult life circumstances is often possible by shifting one’s inner attitudes and by reducing unrealistic expectations and unhelpful reactions. When the practitioner engages these tendencies with a view of kindness toward one’s self, these practices work to strengthen the determination to replace negative and damaging thought patterns with more constructive and realistic viewpoints.

→ Class Meeting 6 -- Module IV: Cultivating Impartiality

Humans are intrinsically social creatures, so attitudes toward others are of great importance. By examining the tendency to place people into in-groups and out-groups based on temporary and subjective criteria, practitioners consider how such categories are both artificial and fluctuating. By contemplating that people – on the most basic level – share a common humanity, the practitioner learns to see that the desire for personal fulfillment and the wish to avoid distress and dissatisfaction is a shared aspiration.

→ Class Meeting 7 -- Module V: Appreciation and Affection for Others

This module begins by recognizing that everything that helps one to thrive and flourish is dependent upon countless others, and this understanding inspires appreciation for those responsible. By attuning to this interconnected ecosystem, a sense of gratitude toward others is engendered. The practitioner moves away from the narrow view of independence and isolation that maintains a self-centered mindset. Through reflection on the daily and long-term gifts of the broader society, and the drawbacks of self-focused attitudes and actions, deep affection is cultivated for others.

→ Class Meeting 8 - Module VI: Empathy and Engaged Compassion

With the perspectives of seeing each person as equally deserving of happiness and as having great value in their own right, practitioners place their attention on the difficulties and distress experienced by so many, which naturally invokes an empathic response. When supported by the inner strength developed in earlier modules, this empathy leads to the strong wish to see others free of difficulties and distress and to orient one’s core motivation toward the alleviation of the suffering

of others.

### **Cancer Health Education (attention control)**

The cancer health education (CHE) intervention is an adaptation of the in-person attention control program called Health Discussion, a protocol used by our group previously.<sup>31</sup> The CHE will focus on relevant topics to health and cancer including 1) cancer advocacy, 2) health and cancer biology, 3) nutrition, 4) lifestyle interventions such as physical activity and goals for physical activity, 5) the importance of good sleep, 6) the impact of stress, and 7) mental health and social support. CHE will also discuss current events related to cancer (e.g. “cancer in the news”), trends about cancer diagnoses, and the latest science and research about cancer (e.g. the Cancer Moonshot).

Over the course of 8 weeks there will be a total of 8 sessions, one session per week, similar to CBCT®. Each session will last for approximately 90 minutes. We will train a public health graduate student to administer the cancer health education attention control per established protocol used previously by prior members of the study team (Badger & Segrin). **ADDIN EN.CITE** <sup>84,85</sup> Through previous experience with the Health Discussion group, we found that public health graduate students have the communication skills, enthusiasms, and scholarly background to teach rigorous attention control groups.<sup>31</sup>

- **Assessments - 8 weeks**

Within a week of concluding the study interventions we will schedule all survivor-caregiver dyads to return to the College of Nursing for the 8-week assessment. The 8-week assessment will mirror the baseline assessment except for the healthcare utilization questionnaire, which will use an 8-week version of this questionnaire (see Appendix).

- **Assessments - 3 months**

About 4 weeks later we will have all survivor-caregiver dyads visit the College of Nursing for the final, 3-month assessment time point. As with the 8-week assessment, this visit will mirror the baseline assessment except for a different healthcare utilization questionnaire, which will use an 3-month version of this questionnaire (see Appendix). At this assessment we will also ask participant to complete and height and weight questionnaire form.

### **Statistical Analytic Plan**

Questionnaire total scores, biomarker data, and other relevant endpoints (e.g. class attendance) will be entered into the study database and managed in SPSS.

Feasibility will be measured by rates of consent and retention of dyads. Acceptability will be measured weekly at each CBCT® session by adherence to program engagement requirements (class attendance, home practice) by both dyadic members. Satisfaction and what participants consider strengths and weaknesses of the program will be assessed immediately post the 8-week intervention.

We will also assess different dimensions of health-related quality of life (HRQOL) before, after, and again 8 weeks after either CBCT® or the cancer health education (CHE) control. The randomized design will yield estimates of the effect sizes for improvements in primary outcomes of physical, psychological, and social HRQOL (depressive symptoms, anxiety, negative affect, fatigue, empathy, and dyadic function) for each member of the dyad for CBCT® versus the control.

The Actor-Partner Interdependence Model will be used to guide exploration of the interdependence over time of the primary outcomes of psychological, physical, and social well-being as well as stress biomarkers in cancer survivors and their informal caregivers.

- ADDIN EN.REFLIST 1. NCI. SEER Cancer Statistics Review (CSR) 1975-2014. 2017; [https://seer.cancer.gov/csr/1975\\_2014/](https://seer.cancer.gov/csr/1975_2014/). Accessed 28 August 2017, 2015.
2. Tung HY, Chao TB, Lin YH, Wu SF, Lee HY, Ching CY, Hung KW, Lin TJ. Depression, Fatigue, and QoL in Colorectal Cancer Patients During and After Treatment. *West J Nurs Res*. 2016;38(7):893-908.
  3. Lowery AE, Krebs P, Coups EJ, Feinstein MB, Burkhalter JE, Park BJ, Ostroff JS. Impact of symptom burden in post-surgical non-small cell lung cancer survivors. *Support Care Cancer*. 2014;22(1):173-180.
  4. Sullivan DR, Forsberg CW, Ganzini L, Au DH, Gould MK, Provenzale D, Lyons KS, Slatore CG. Depression symptom trends and health domains among lung cancer patients in the CanCORS study. *Lung Cancer*. 2016;100:102-109.
  5. Watts S, Leydon G, Birch B, Prescott P, Lai L, Eardley S, Lewith G. Depression and anxiety in prostate cancer: a systematic review and meta-analysis of prevalence rates. *BMJ Open*. 2014;4(3):e003901.
  6. Fann JR, Thomas-Rich AM, Katon WJ, Cowley D, Pepping M, McGregor BA, Gralow J. Major depression after breast cancer: a review of epidemiology and treatment. *Gen Hosp Psychiatry*. 2008;30(2):112-126.
  7. Krebber AM, Buffart LM, Kleijn G, Riepma IC, de Bree R, Leemans CR, Becker A, Brug J, van Straten A, Cuijpers P, Verdonck-de Leeuw IM. Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments. *Psychooncology*. 2014;23(2):121-130.
  8. Schneider EC, Malin JL, Kahn KL, Ko CY, Adams J, Epstein AM. Surviving colorectal cancer : patient-reported symptoms 4 years after diagnosis. *Cancer*. 2007;110(9):2075-2082.
  9. Iyer S, Taylor-Stokes G, Roughley A. Symptom burden and quality of life in advanced non-small cell lung cancer patients in France and Germany. *Lung Cancer*. 2013;81(2):288-293.
  10. Colloca G, Venturino A, Governato I, Checcaglini F. Incidence and Correlates of Fatigue in Metastatic Castration-Resistant Prostate Cancer: A Systematic Review. *Clin Genitourin Cancer*. 2016;14(1):5-11.
  11. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: the scale of the problem. *Oncologist*. 2007;12 Suppl 1:4-10.
  12. Lawrence DP, Kupelnick B, Miller K, Devine D, Lau J. Evidence report on the occurrence, assessment, and treatment of fatigue in cancer patients. *J Natl Cancer Inst Monogr*. 2004(32):40-50.
  13. Curt GA, Breitbart W, Cella D, Groopman JE, Horning SJ, Itri LM, Johnson DH, Miaskowski C, Scherr SL, Portenoy RK, Vogelzang NJ. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. *Oncologist*. 2000;5(5):353-360.

14. Saboonchi F, Petersson LM, Wennman-Larsen A, Alexanderson K, Vaez M. Trajectories of Anxiety Among Women with Breast Cancer: A Proxy for Adjustment from Acute to Transitional Survivorship. *J Psychosoc Oncol*. 2015;33(6):603-619.
15. Maass SW, Roorda C, Berendsen AJ, Verhaak PF, de Bock G. The prevalence of long-term symptoms of depression and anxiety after breast cancer treatment: A systematic review. *Maturitas*. 2015;82(1):100-108.
16. Eisenberg SA, Kurita K, Taylor-Ford M, Agus DB, Gross ME, Meyerowitz BE. Intolerance of uncertainty, cognitive complaints, and cancer-related distress in prostate cancer survivors. *Psychooncology*. 2015;24(2):228-235.
17. Custers JA, Gielissen MF, Janssen SH, de Wilt JH, Prins JB. Fear of cancer recurrence in colorectal cancer survivors. *Support Care Cancer*. 2016;24(2):555-562.
18. Braamse AM, van Turenhout ST, Terhaar Sive Droste JS, de Groot GH, van der Hulst RW, Klemm-Kropp M, Kuiken SD, Loffeld RJ, Uiterwaal MT, Mulder CJ, Dekker J. Factors associated with anxiety and depressive symptoms in colorectal cancer survivors. *Eur J Gastroenterol Hepatol*. 2016;28(7):831-835.
19. Li QP, Mak YW, Loke AY. Spouses' experience of caregiving for cancer patients: a literature review. *Int Nurs Rev*. 2013;60(2):178-187.
20. Segrin C, Badger TA. Psychological distress in different social network members of breast and prostate cancer survivors. *Res Nurs Health*. 2010;33(5):450-464.
21. Kent E, Rowland, JH, Northouse, L, Litzelman, K, Chou, WS, Shelburne, N, Timura, C, O'Mara, A, Huss, K. Caring for caregivers and patients: Research and clinical priorities for informal cancer caregiving. *Cancer*. 2016:1-9.
22. Northouse L, McCorkle, R. Spouse Caregivers of Cancer Patients. In: Holland JC BW, Butow PN, Jacobsen PB, Loscalzo MJ, McCorkle R, ed. *Psycho-Oncology*. 3rd ed. New York: Oxford University Press; 2015:567-578.
23. Litzelman K, Kent EE, Mollica M, Rowland JH. How Does Caregiver Well-Being Relate to Perceived Quality of Care in Patients With Cancer? Exploring Associations and Pathways. *J Clin Oncol*. 2016.
24. Segrin C, Badger TA. Psychological and physical distress are interdependent in breast cancer survivors and their partners. *Psychol Health Med*. 2014;19(6):716-723.
25. Segrin C, Badger TA, Harrington J. Interdependent psychological quality of life in dyads adjusting to prostate cancer. *Health Psychol*. 2012;31(1):70-79.
26. Hatfield E, Cacioppo JT, Rapson RL. *Emotional contagion*. Cambridge, MA: Cambridge University Press; 1994.
27. Dodds SE, Pace TW, Bell ML, Fiero M, Negi LT, Raison CL, Weihs KL. Feasibility of Cognitively-Based Compassion Training (CBCT) for breast cancer survivors: a randomized, wait list controlled pilot study. *Support Care Cancer*. 2015;23(12):3599-3608.
28. Mascaro JS, Rilling JK, Tenzin Negi L, Raison CL. Compassion meditation enhances empathic accuracy and related neural activity. *Soc Cogn Affect Neurosci*. 2013;8(1):48-55.
29. Pace TW, Negi LT, Dodson-Lavelle B, Ozawa-de Silva B, Reddy SD, Cole SP, Danese A, Craighead LW, Raison CL. Engagement with Cognitively-Based Compassion Training is associated with reduced salivary C-reactive protein from before to after training in foster care program adolescents. *Psychoneuroendocrinology*. 2012.
30. Reddy SD, Negi LT, Dodson-Lavelle B, Ozawa-de Silva B, Pace TWW, Cole SP, Raison CL, Craighead LW. Cognitively-based Compassion Training: A promising prevention strategy for at-risk adolescents. *Journal of Child and Family Studies*. 2012;22(2):219-230.
31. Desbordes G, Negi LT, Pace TW, Wallace BA, Raison CL, Schwartz EL. Effects of mindful-attention and compassion meditation training on amygdala response to emotional stimuli in an ordinary, non-meditative state. *Front Hum Neurosci*. 2012;6:292.

32. Pace TWW, Negi LT, Sivilli TI, Issa MJ, Cole SP, Adame DD, Raison CL. Innate immune, neuroendocrine and behavioral responses to psychosocial stress do not predict subsequent compassion meditation practice time. *Psychoneuroendocrinology*. 2010;35(2):310-315.
33. Pace TW, Negi LT, Adame DD, Cole SP, Sivilli TI, Brown TD, Issa MJ, Raison CL. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. *Psychoneuroendocrinology*. 2009;34(1):87-98.
34. Sethi G, Sung B, Aggarwal BB. Nuclear factor-kappaB activation: from bench to bedside. *Experimental Biology & Medicine*. 2008;233(1):21-31.
35. Miller AH, Ancoli-Israel S, Bower JE, Capuron L, Irwin MR. Neuroendocrine-immune mechanisms of behavioral comorbidities in patients with cancer. *Journal of Clinical Oncology*. 2008;26(6):971-982.
36. Collado-Hidalgo A, Bower JE, Ganz PA, Irwin MR, Cole SW. Cytokine gene polymorphisms and fatigue in breast cancer survivors: early findings. *Brain Behav Immun*. 2008;22(8):1197-1200.
37. Bower JE. Prevalence and causes of fatigue after cancer treatment: the next generation of research. *J Clin Oncol*. 2005;23(33):8280-8282.
38. Bower JE, Ganz PA, Aziz N, Fahey JL. Fatigue and proinflammatory cytokine activity in breast cancer survivors. *Psychosomatic Medicine*. 2002;64(4):604-611.
39. Bower JE, Ganz PA, Tao ML, Hu W, Belin TR, Sepah S, Cole S, Aziz N. Inflammatory biomarkers and fatigue during radiation therapy for breast and prostate cancer. *Clin Cancer Res*. 2009;15(17):5534-5540.
40. Wratten C, Kilmurray J, Nash S, Seldon M, Hamilton CS, O'Brien PC, Denham JW. Fatigue during breast radiotherapy and its relationship to biological factors. *Int J Radiat Oncol Biol Phys*. 2004;59(1):160-167.
41. Collado-Hidalgo A, Bower JE, Ganz PA, Cole SW, Irwin MR. Inflammatory biomarkers for persistent fatigue in breast cancer survivors. *Clin Cancer Res*. 2006;12(9):2759-2766.
42. Musselman DL. Higher than normal plasma interleukin-6 concentrations in cancer patients with depression: preliminary findings. *American Journal of Psychiatry*. 2001;158(8):1252-1257.
43. Torres MA, Pace TW, Liu T, Felger JC, Mister D, Doho GH, Kohn JN, Barsevick AM, Long Q, Miller AH. Predictors of depression in breast cancer patients treated with radiation: role of prior chemotherapy and nuclear factor kappa B. *Cancer*. 2014;119(11):1951-1959.
44. Geinitz H, Zimmermann FB, Stoll P, Thamm R, Kaffenberger W, Ansorg K, Keller M, Busch R, van Beuningen D, Molls M. Fatigue, serum cytokine levels, and blood cell counts during radiotherapy of patients with breast cancer. *Int J Radiat Oncol Biol Phys*. 2001;51(3):691-698.
45. Pall ML. Post-radiation syndrome as a NO/ONOO- cycle, chronic fatigue syndrome-like disease. *Med Hypotheses*. 2008;71(4):537-541.
46. Torres MA, Liu T, Chen H, Godette K, Mister D, Pace TWW, Miller AH. A Prospective Study of Cancer- Related Fatigue in Women Undergoing Radiotherapy for Breast Cancer. *Int J Rad Bio Phys*. 2011;81:S129.
47. Bierhaus A, Wolf J, Andrassy M, Rohleder N, Humpert PM, Petrov D, Ferstl R, von Eynatten M, Wendt T, Rudofsky G, Joswig M, Morcos M, Schwaninger M, McEwen B, Kirschbaum C, Nawroth PP. A mechanism converting psychosocial stress into mononuclear cell activation. *Proceedings of the National Academy of Sciences of the United States of America*. 2003;100(4):1920-1925.
48. Steptoe A, Hamer M, Chida Y. The effect of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. *Brain, Behavior, & Immunity*. 2007;21(7):901-912.
49. Segerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychol Bull*. 2004;130(4):601-630.

50. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. *Nature reviews neuroscience*. 2008;9(1):46-56.
51. Bower JE. Cancer-related fatigue--mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol*. 2014;11(10):597-609.
52. Fagundes C1, 3, LeRoy A4, Karuga M5. Behavioral symptoms after breast cancer treatment: A biobehavioral approach. *Journal of Perspective Medicine*. 2015;5(3):280-295.
53. Spiegel DG-D, J. Depression and cancer: Mechanisms and Disease Progression. *Society of Biological Psychiatry*. 2003;54:269-282.
54. Spiegel D, Giese-Davis J, Taylor CB, Kraemer H. Stress sensitivity in metastatic breast cancer: analysis of hypothalamic-pituitary-adrenal axis function. *Psychoneuroendocrinology*. 2006;31(10):1231-1244.
55. Giese-Davis J, Spiegel D. Emotional expression and cancer progression. *Handbook of affective sciences*. 2003(Journal Article):1053–1082.
56. Giese-Davis J, Wilhelm FH, Conrad A, Abercrombie HC, Sephton S, Yutsis M, Neri E, Taylor CB, Kraemer HC, Spiegel D. Depression and stress reactivity in metastatic breast cancer. *Psychosomatic medicine*. 2006;68(5):675-683.
57. Giese-Davis J, Collie et al. . Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: A secondary analysis. *Journal of clinical oncology*. 2010;29(4):413-420.
58. Bower JE GP, Dickerson SS, Peterson L, Azia N, & Fahey JL. Diurnal cortisol rhythm and fatigue in breast cancer survivors. *PsychoNeuroendocrinology*. 2005;30:92-100.
59. Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. Diurnal cortisol rhythm as a predictor of breast cancer survival.[see comment]. *Journal of the National Cancer Institute*. 2000;92(12):994-1000.
60. Chida Y, Hamer M, Wardle J, Steptoe A. Do stress-related psychosocial factors contribute to cancer incidence and survival? *Nat Clin Pract Oncol*. 2008;5(8):466-475.
61. Jarcho MR SG, Tylova-Stein H, Wolkowitz OM, Burke HM. Dysregulated diurnal cortisol pattern is associated with glucocorticoid resistance in women with major depressive disorder. . *Biological Psychology*. 2013;93(1):150-158.
62. Spiegel D, Giese-Davis, J., Taylor, C.B., & Kraemer, H. Stress sensitivity in metastatic breast cancer: Analysis of the hypothalamic-pituitary-adrenal axis function. *PsychoNeuroendocrinology*. 2006;31:1231-1244.
63. Giese-Davis J, Sephton SE, Abercrombie HC, Duran RE, Spiegel D. Repression and high anxiety are associated with aberrant diurnal cortisol rhythms in women with metastatic breast cancer. *Health Psychology*. 2004;23(6):645-650.
64. Abercrombie HC, Giese-Davis J, Sephton S, Epel ES, Turner-Cobb JM, Spiegel D. Flattened cortisol rhythms in metastatic breast cancer patients. *Psychoneuroendocrinology*. 2004;29(8):1082-1092.
65. Turner-Cobb JM, Sephton SE, Koopman C, Blake-Mortimer J, Spiegel D. Social support and salivary cortisol in women with metastatic breast cancer. *Psychosomatic Medicine*. 2000;62(3):337-345.
66. Thornton LM AB, Blakely WP. The pain, depression, and fatigue symptom cluster in advanced breast cancer: covariation with the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system. *Health Psychology*. 2010;29(3):333-337.
67. PROMIS. Adult Depression version 1.0 short form: a brief guide to the 8-item PROMIS Short Form v1.0-Depression 8b. 2012. 2012.
68. PROMIS. Adult satisfaction with participation in social roles profile short forms. 2013. 2013.
69. PROMIS. Adult physical function profile short forms. 2013. 2013.

70. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, Amtmann D, Bode R, Buysse D, Choi S, Cook K, Devellis R, DeWalt D, Fries JF, Gershon R, Hahn EA, Lai JS, Pilkonis P, Revicki D, Rose M, Weinfurt K, Hays R. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*. 2010;63(11):1179-1194.
71. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988;54(6):1063-1070.
72. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, Huber SL. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer*. 1999;85(5):1186-1196.
73. Pulos S, Elison J, Lennon R. The hierarchical structure of the Interpersonal Reactivity Index. *Social Behavior and Personality*. 2004;32:355-359.
74. Davis MH. Measuring individual differences in empathy: evidence for a multi-dimensional approach. *Journal of Personality and Social Psychology*. 1983;44:113-126.
75. Davis MH. *Empathy: A social psychological approach*. Boulder, Colorado: Westview Press; 1994.
76. Lee RM, Robbins SB. Measuring belongingness: The Social Connectedness and Social Assurance Scales. *Journal of Counseling Psychology*. 1995;42:232-241.
77. Lee RM, Draper M, Lee S. Social connectedness, dysfunctional interpersonal behaviors, and psychological distress: Testing a mediator model. *Journal of Counseling Psychology*. 2001;48(3):310-318.
78. Hendrick SS. A generic measure of relationship satisfaction. *Journal of Marriage and the Family*. 1988;50:93-98.
79. Neff KD. Development and validation of a scale to measure self-compassion. *Self and Identity*. 2003;2:223-250.
80. Breines JG, Thoma MV, Gianferante D, Hanlin L, Chen X, Rohleder N. Self-compassion as a predictor of interleukin-6 response to acute psychosocial stress. *Brain Behav Immun*. 2014;37:109-114.
81. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA*. 1995;273(1):59-65.
82. Negi LT. *Emory Compassion Meditation Protocol: Cognitively-Based Compassion Training Manual*. . Atlanta, GA: Emory University; 2013.
83. Ozawa-de Silva B, Dodson-Lavelle B, Raison CL, Negi LT. Compassion and ethics: Scientific approaches to the cultivation of compassion as a foundation for ethical subjectivity and well-being. . *Journal of Healthcare, Science, and the Humanities*. 2012;11(1):145-157.
84. Badger TA, Segrin C, Figueredo AJ, Harrington J, Sheppard K, Passalacqua S, Pasvogel A, Bishop M. Psychosocial interventions to improve quality of life in prostate cancer survivors and their intimate or family partners. *Qual Life Res*. 2011;20(6):833-844.
85. Badger TA, Segrin C, Hepworth JT, Pasvogel A, Weihs K, Lopez AM. Telephone-delivered health education and interpersonal counseling improve quality of life for Latinas with breast cancer and their supportive partners. *Psychooncology*. 2013;22(5):1035-1042.

## 9) Cost to subjects

There are no costs to be in this study, except for subjects' time. The total time commitment will be about 14 hours, over a 3 month period.



## 10) Risks to subjects

Subjects may be uncomfortable discussing their cancer and its treatment and how they cope with their cancer diagnosis and treatment. If they become too anxious or upset by discussing cancer treatment or its side effects, they will be able to stop at any time. To minimize risk, subjects will be asked to inform study staff if their levels of emotional distress increase during the telephone assessments. They will not have to answer any questions that upset them.

The questions subjects answer during the assessments will contain personal information. There is a risk that this information could become public, or fall into the hands of someone not associated with the study. We will take steps to prevent this from happening (see below).

We will refer to the appropriate social service agency or cancer advocacy organization in the community.

There are also risks associated with blood sampling by venipuncture. These risks include discomfort and a slight risk for infection, bruising and/or bleeding at the blood draw site. To minimize risks associated with the blood draw, the procedure will be done in a sterile manner by a phlebotomist trained and experienced in venipuncture.

## 11) Potential benefits to subjects and/or society

Participants may benefit from the intervention programs that are part of this study. Both CHE and CBCT® are designed to impart useful skills to program participants (see interventions descriptions above). The participation of subjects may also ultimately help improve psychosocial health care for women who are survivors of breast cancer by investigating the benefits of two programs that could eventually be made available to all cancer survivors and informal caregivers.

## 12) Provisions to protect the privacy of subjects and the confidentiality of data

- a. **Protection of subject privacy:** The identity of subjects will be protected during recruitment and consenting by holding meetings at location that are reasonably private, although they may be public buildings, for example a quiet area at a community center. Participants will be asked to only complete study assessments (baseline, 8-week, 3-month) while in a private setting at the College of Nursing.
- b. **Protection of data confidentiality:** All study material including source documents and casebooks will be stored in a secured room (either Dr. Pace's office, College of Nursing 443, Ms. Figueroa's office, College of Nursing 441, or the Office of Nursing Research, College of Nursing 410) or on a secure computer server or personal computer that are HIPAA compliant and can only be accessed by study researchers. Data collected during the telephone assessments and the research center visit will be stored by study number, not by subject name. A paper copy list linking subject names to their subject numbers will be stored in a locked drawer located inside Dr. Pace's office at the College of Nursing.

### **13) Access to Private Information**

- a. **Access to medical records (HIPAA):** n/a. This study will not access medical records of participants, electronic or otherwise.

### **14) Subject compensation**

Participant dyads (cancer survivors and informal partners) will receive \$20 for each intervention session they attend, as well as \$20 for each assessment visit attended. The maximum compensation that a dyad can receive in this study is \$220.

### **15) Medical care and compensation for injury**

In the event of injury we will arrange for emergency care, and at the nearby Banner UMC if necessary. A participant and/or their insurance company will be billed for the cost of this care. We have not set aside any funds to compensate participants for illness or injury. The exception would be if it is proven that the illness or injury in a participant was a direct result of negligence (not fulfilling a standard duty) on the part of a University of Arizona employee.

### **16) Monitoring for subject safety**

It is possible that some of the participants may develop psychiatric and/or medical problems from screening to enrollment to after study end (up to 3 months later). Also, although not expected, it is possible that blood draws may result in adverse events for some participants. For these reasons we have elected to use the Data Safety Monitoring Board (DSMB) at the University of Arizona College of Nursing for this study. The purpose of the UACoN DSMB is to provide UA researchers easier access to and utilization of a data and safety monitoring board for investigator-initiated human research studies for which there is not a DSMB already appointed. This DSMB will provide independent oversight to further promote the protection of human subjects and the overall integrity of the study. The DSMB will meet once every six months. This protocol will be submitted to the DSMB simultaneously with this initial submission to the University of Arizona IRB. The DSMB will review the research protocol and plans for data and safety monitoring. Once every 6 months the DSMB will review a report from the study's data manager (Dr. Szalacha) that includes: the number of participants who signed consent for the study, the number of dropouts, reasons for these dropouts, and any safety concerns, adverse events, an up-to-date consent form, and measures taken to protect confidentiality (e.g., data storage, use of coded ID numbers, etc.). The DSMB will also review the Principal Investigator's summary of any new data or evidence that might alter the risk/benefit ratio for participating in the study (e.g., newly published studies, etc.). After reviewing this information, the DSMB will issue its own report summarizing any serious and unexpected adverse events or other unanticipated problems that involve risk to study participants, and whether these appear related to the study-based research assessment protocol. There will be regular, ongoing communication between the PI, the University of Arizona IRB, and the DSMB. The PI will take responsibility for reporting any serious and unexpected adverse events or other unanticipated study problems to the University of Arizona IRB within 24 hours, and the sponsor according to standard regulations. A copy

of this correspondence will be sent to the DSMB. Actions taken by the IRB or the study sponsor in response to adverse event reports will be immediately reported to the DSMB.

#### 17) Withdrawal of subjects

Subjects may withdraw whenever they wish, and they may be removed from the study at the discretion of the Principle Investigator if they are found to not meet inclusion/ exclusion criteria, or if they experience excessive medical or psychological distress. The PI will be available in the event that withdrawal is necessary, and will refer subjects to appropriate care resources including nearby medical facilities. We will continue to follow-up with subjects if withdrawal is necessary to make sure they have received appropriate care.

#### 18) Sharing of results with subjects

If requested by subjects, we will share their study information with them, as well as overall study findings/ manuscripts/ publications that contain aggregate information but no identifiable information from other study subjects.

#### 19) Future use and long-term storage of data or specimens

Data will not be kept beyond the study period, including blood samples that will be collected.

#### 20) Information management

Not applicable.

#### 21) Clinical Trials.gov Information

- ☒ [ClinicalTrials.gov](https://clinicaltrials.gov) "NCT" number for this trial (provide): NCT03459781
- ☐ Registration pending
- ☐ Clinical trial does not require registration (explain):

#### 22) Gases

Not applicable

**SECTION 4: LIST OF ATTACHMENTS FOR THIS SUBMISSION (REQUIRED)** (Items listed here are expected to be attached as separate documents. These documents will appear in the UA HSPP IRB approval letter as 'documents submitted concurrently' with the review.)

Document Name	Version Date

See HSPP website for submission requirements.

**Items needed for approval:**

- Word Versions of Application, Consents, Recruitment and Data Collection
- **F107: Verification of Training Form**
- **Current PI/Co-PI CVs or biosketch**, if not included with copy of grant application
- **Informed Consent/Permission/Assent Form(s)** – including study specific release of information documents, DHHS approved sample consent forms. If consent will not be documented in writing, a script of information to be provided orally to subjects

**Other Items as applicable:**

- **Appendix A - Children**
- **Appendix B - Drug/Device**
- **Appendix C- Multi Site Research**
- **Appendix D- Pregnant Women and Neonates**
- **Appendix E- Prisoners**
- **Appendix F- Waiver of Consent/ PHI**
- **Appendix G- Exception from Informed Consent (EFIC)**
- **Appendix H- Native American**
- **Biosafety Review letter** (for UA - Institutional Biosafety Committee)
- **Certificate of Confidentiality**
- **Compressed Gases Review letter** (for UA – Research Instrumentation)
- **Contract** – complete or draft copy of contract including budget
- **Data Collection Tools** – surveys, questionnaires, diaries not included in the protocol, data abstraction form for records review
- **Data Monitoring Charter and Plan**
- **Drug/Device information** – Investigator's Brochure, drug product sheet, device manual, user's manual, instructions for use, package insert, IND/IDE documentation, FDA 1572 form, 510k indication, FDA exemption, sponsor determination of device risk, etc.
- **Export Control Review**
- **Grant Application(s)** – cover-to-cover copy of grant, regardless of home institution or funding agency, and a copy of the Notice of Grant Award.
- **Multi-site information** (for sites engaged in research where the UA is the IRB of record)
  - o Copy of any approvals granted from that site (including determinations if this site has an IRB of its own)
  - o Site-specific F107
  - o Copy of the site's human subjects training policy
  - o CV and medical license (if applicable) of site PI
- **Other Approval letters** (e.g., school districts, Tribal, other IRB approvals)
- **Participant Materials** – written materials to be provided to or meant to be seen or heard by subjects (e.g. study newsletter, physician to participant letter, wallet cards, incentive items, holiday/birthday cards, certificates, instructional videos/written guides, calendars, certification of achievement, etc.)
- **Payer coverage analysis**
- **PHI Authorization Form(s)**
- **Protocol** – including all amendments/revisions, sub- or extension-studies
- **Radiation Safety Review letter**- needed regardless if the radiation device is approved and used standard of care
- **Recruitment Materials** – telephone scripts, flyers, brochures, websites, email texts, radio/television spots, newspaper advertisements, press releases, etc.
- **Scientific Review Committee letter** (for cancer related projects – AZCC SRC; other units as applicable if the unit has a scientific review committee)
- **Site Authorizations** for research purposes and/or access to administrative records/samples
  - o External sites (such as schools, other hospitals or campuses, etc.)
  - o UAHS Research Portal feasibility review approval
- **Travel Authorization documentation** (for UA – Office of Global Initiatives)
- **Use of retrospective research samples and/or data** – IRB approval letter, original consent under which samples/data were collected, letter allowing access to samples